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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/507,139	09/09/2004	Darren Mark Le Grand	PR/4-32412A	8975

1095 7590 10/02/2006

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CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
CHUNG, SUSANNAH LEE	
ART UNIT	**PAPER NUMBER**
1626	

DATE MAILED: 10/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/507,139	LE GRAND ET AL.	
	Examiner	Art Unit	
	Susannah Chung	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 18-28* is/are pending in the application.

4a) Of the above claim(s) *8 and 18-21* is/are withdrawn from consideration.

5)☒ Claim(s) *1-7,9,10,22-25 and 28* is/are allowed.

6)☒ Claim(s) *26 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/9/04, 1/4/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-10 and 18-28 are pending in the instant application.

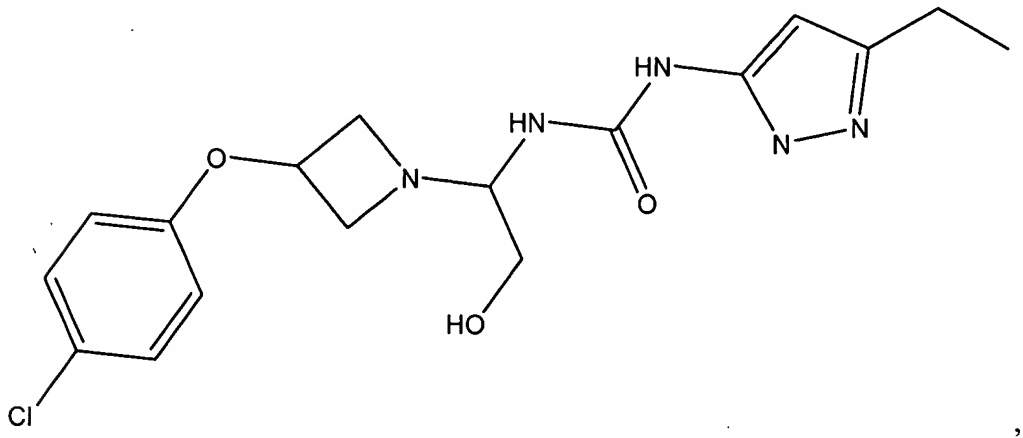
Priority

This application is a 371 of PCT/EP03/02715, filed 03/14/2003.

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d) by application nos. 0206218.0 and 0229627.5 filed in the United Kingdom Patent Office on 03/15/2002 and 12/19/2002, which papers have been placed of record in the file.

Response to Election/Restrictions

Applicant's election *without traverse* of Group I in the reply filed on 25 August 2006 is acknowledged. Further, the election of species of the compound of Example 88 on page 38, N-3-[3-(4-chlorophenoxy)-1-azetidinyl)-1-(hydroxymethyl)propyl]-N'-[3-ethyl-1H-pyrazol-5-yl]-urea,



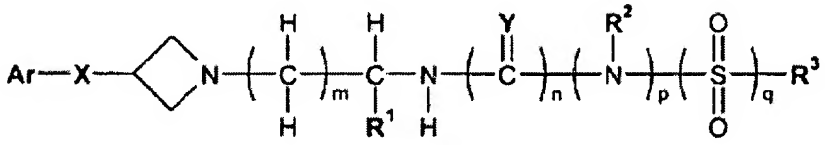
, of the specification is acknowledged.

Scope of the Elected Invention

Claims 1-10 and 18-28 are pending in this application.

The scope of the elected subject matter that will be examined and searched is as follows:

Compounds of formula (I),



, depicted in claim 1, page 2, wherein:

Ar is phenyl optionally substituted by one or more substituents selected from halogen, C_1-C_8-alkyl, cyano or nitro;

R^1 is hydrogen or C_1-C_8-alkyl optionally substituted by hydroxy, C_1-C_8-alkoxy,

R^2 is hydrogen, C_1-C_8-alkyl or C_3-C_{10}-cycloalkyl and R^3 is C_1-C_8-alkyl substituted by phenyl, phenoxy, acyloxy or naphthyl,

Y is oxygen

R^3 is C_1-C_8-alkyl substituted by phenyl,

m is 2;

n is 1;

p is 1; and

q is 0.

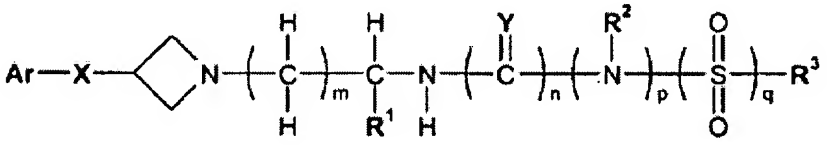
Scope of Withdrawn Subject Matter

Claims 8, 18-21, 26-28 are withdrawn from further consideration by the examiner, 37 C.F.R. §1.142(b), as being drawn to a non-elected invention. The withdrawn subject matter is patentably distinct from the elected subject matter as it differs in structure and

element and would require separate search considerations. In addition, a reference, which anticipates one group, would not render obvious the other.

The scope of the withdrawn subject matter that will not be examined and searched is as follows:

Compounds of formula (I),



, depicted in claim 1, page 2, wherein:

R^1 is

carboxy, C_1-C_8-alkoxycarbonyl, -N(R^*)R^5, -CON(R^6)R^7 or by a monovalent cyclic organic group having 3 to 15 atoms in the ring system;

R^3 is C_3-C_{10}-cycloalkyl optionally having a benzo group fused thereto, a heterocyclic group having 5 to 11 ring atoms of which 1 to 4 are hetero atoms, phenyl or naphthyl, said phenyl, phenoxy or naphthyl groups being optionally substituted by one or more substituents selected from halogen, cyano, hydroxy, acyl, nitro, -SO_2NH_2, C_1-C_8-alkyl optionally substituted by C_1-C_8-alkoxy, C_1-C_8-haloalkyl, C_1-C_8-alkoxy, C_1-C_8-haloalkoxy, C_1-C_8-alkylthio, -SO_2-C_1-C_8-alkyl, C_1-C_8-alkoxycarbonyl, C_1-C_8-acylamino optionally substituted on the nitrogen atom by C_1-C_8-alkyl, C_1-C_8-alkylamino, aminocarbonyl, C_1-C_8-alkylamino-carbonyl, di(C_1-C_8-alkyl)amino, di(C_1-C_8-alkyl)aminocarbonyl, di(C_1-C_8-alkyl)aminocarbonyl-methoxy, or R^2 and R^3 together with the nitrogen atom to which they are attached denote a heterocyclic group having 5 to 10 ring atoms of which 1, 2 or 3 are hetero atoms;

Y is sulfur;

m is 1, 3, or 4;

n is 0;

p is 0; and

q is 1+.

Scope Expanded - Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-8 and 18-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Taylor, et al (U.S. Pat. No. 5,095,014 (1992)).

Applicants claims of substituted azetidine compounds relate to compound of Formula (I) in claim 1. Taylor discloses compounds in claim 1 that anticipate the instantly claimed genus wherein: Ar is phenyl optionally substituted, m is 0, R1 is hydroxyl, n is 0, p is 1, R2 is H, q is 0 and R3 is allyl.

Rejoinder

Claims 1-7, 9-10, 22-25 are directed to an allowable product. Pursuant to the procedures set forth in MPEP § 821.04(B), claims 26-28, directed to the process of making or using an allowable product, previously withdrawn from consideration as a result of a restriction requirement, are hereby rejoined and fully examined for patentability under 37 CFR 1.104.

Because all claims previously withdrawn from consideration under 37 CFR 1.142 have been rejoined, **the restriction requirement as set forth in the Office action mailed on 7/26/2006 is hereby withdrawn**. In view of the withdrawal of the restriction requirement as to the rejoined inventions, applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be

subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Once the restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 26 and 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement because the specification does not enable one skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims, for the reasons describe below.

As stated in MPEP 2164.01(a), "there are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

The factors to be considered when determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, were described in In re Wands, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) as:

1. the nature of the invention;
2. the breadth of the claims;
3. the state of the prior art;

4. the relative skill of those in the art;

5. the predictability or unpredictability of the art;

6. the amount of direction or guidance presented [by the inventor];

7. the presence or absence of working examples; and

8. the quantity of experimentation necessary [to make and/or use the invention].

The eight Wands factors are applied to Claims 26 and 27 of the present invention below:

(1) The Nature of the Invention

Claim 26. (Withdrawn) A method of treating a condition mediated by CCR-3 in a subject in need of such treatment, which comprises administering to said subject an effective amount of a compound of formula I as defined in claim 1 in free form or in the form of a pharmaceutically acceptable salt.

Claim 27. (Withdrawn) A method of treating an inflammatory or obstructive airways disease in a subject in need of such treatment, which comprises administering to said subject an effective amount of a compound of formula I as defined in claim 1 in free form or in the form of a pharmaceutically acceptable salt.

(2) The Breadth of the claims

Claims 26 and 27 will be give its broadest reasonable interpretation. The applicable rule for interpreting the claims is that "each claim must be separately analyzed and given its broadest reasonable interpretation in light of and consistent with the written description." See MPEP 2163(II)(1), citing In re Morris, 127 F.3d 1048, 1053-1054; 44 USPQ2d 1023, 1027 (Fed. Cir. 1997). In view of this rule, Claims 26 and 27, which do not specify the many possible CCR-3, inflammatory or obstructive airway diseaseswill be

interpreted to encompass all types of allergic and autoimmune diseases, regardless of whether it is a primary or secondary method of use.

(3) The state of the prior art

The state of the art at the time of this application was that no single compound or class of compounds was known to treat all CCR-3, inflammatory or obstructive airway diseases. It is well known in the art that many different receptors, pathways and mechanisms can be used to treat inflammatory or obstructive airway diseases.

(4) The relative skill of those in the art

The level of skill in the art (pharmaceutical chemists, physicians) would be high.

(5) The predictability or unpredictability of the art

It is noted that the pharmaceutical art generally is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement varies inversely with the degree of unpredictability in the factors involved. In re Fisher, 427 F.2d 833, 839. Therefore, the more unpredictable an area, the more specific enablement is needed in order to satisfy the statute. Added to the unpredictability of the art itself is the question whether in vitro activity against CCR-3 by one of the compound of the present invention could be reliably and predictably extrapolated to in vivo activity in patients with all CCR-3, inflammatory and obstructive airways diseases claimed. There is no absolute predictability, even in view of the high level of skill in the art.

(6) The amount of direction or guidance presented (by the inventor)

The specification in the present invention discloses that the compound of the instant application is effective in a CCR-3 binding assay (specification page 21), but fails to show selectivity for any one disorder.

(7) The presence or absence of working examples

As noted in the previous section, the specification discloses the general role of the instantly claimed compounds in CCR-3 binding assays, but does not provide any working examples of the use of the instantly claimed compound in the treatment of a disease.

(8) The quantity of experimentation necessary (to make and/or use the invention)

Given the absence of direction or guidance (or working examples) in the specification for the role of the CCR-3 receptor antagonists of formula (I), it would cause a skilled artisan an undue amount of experimentation to practice this invention to determine which patients with which diseases would benefit from which of the many claimed compounds within the scope of the invention with a reasonable expectation of success.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susannah Chung whose telephone number is (571) 272-6098. The examiner can normally be reached on M-F, 8am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Date: 25 September 2006